Remarks / Arguments

Claims 1-14 and 17-34 are pending in this application.

Claim 18 has been amended herein to correct its dependency. No new matter has been added by way of this amendment.

Applicants respectfully request reconsideration of pending claims 1-14 and 17-34.

The Examiner has requested that the Applicants amend the first line of the application to update the status of the priority application (Office Action, section 3). However, Applicants respectfully draw the Examiner's attention to the March 17, 2003 amendment (Paper No. 47), in which the specification was updated to indicate the abandonment of the priority application (see Paper No. 47, Appendix B).

Additionally, Applicants respectfully request that the Patent Attorney Docket No. be changed from **ALX-149** to **ALX-20 FWC (109488-128)**, as indicated previously in the CPA request filed on May 14, 2003 and the Amendment filed on March 17, 2003.

I. Objection to Under 35 U.S.C. § 132

The Amendment filed November 5, 2001 (Paper No. 37) stands objected to under 35 U.S.C. § 132 as allegedly introducing new matter into the disclosure. The Examiner objects to the amendments to pages 56, 59 and 60 of the specification for failing "to have adequate written description support in the application as-filed" (Office Action, section 4).

Applicants respectfully traverse this objection.

In the Preliminary Amendment, filed on November 5, 2001, Applicants amended the specification to insert text relating to the ability of the 5G1.1 antibody to bind to both the alpha and beta chains of human C5 protein, as determined by immunoblot assay. After entry of this amendment, the text of Example 8 of the instant application exactly corresponds to the text of Example 7 in Wang *et al.* (U.S. Patent No. 6,074,642 (hereafter the '642 patent), columns 18-19, (submitted previously). The Wang *et al.* application (U.S. Serial No. 08/236,208), which evolved into the '642 patent, was incorporated by reference into the specification of the instant application *in its entirety* (see page 6, lines 6-7 and page 60, lines 11-16).

"The information incorporated is as much a part of the application as filed as if the text was repeated in the application, and should be treated as part of the application as filed. Replacement of the identified material incorporated by reference with the actual text is not new matter." (M.P.E.P. § 2163.07(b). See also *Mendenhall v. Astec Industries Inc.,* 13 USPQ2d 1913, 1922 (E.D. Tenn. 1988), aff'd, 887 F.2d 1094, 13 U.S.P.Q.2d 1956 (Fed. Cir. 1989) (unpublished) ("A patent application may comply with 35 U.S.C. § 112 by incorporating by reference the disclosure of another pending United States patent application."); *Ernsthausen v. Nakayama*, 1 U.S.P.Q.2d 1539, 1547 (Bd. Pat. App. & Int'f 1985), *aff'd*, 809 F.2d 787 (Fed. Cir. 1986) (unpublished) ("An application for a patent when filed may incorporate essential material by reference to a United States patent"). Therefore, Applicants have not added new matter to the specification by way of the 05 November 2001 Preliminary Amendment, as the added text was identical to text in a patent application, which was properly incorporated by reference in its entirety in the as-filed application.

Thus, contrary to the Examiner's assertions, no new matter was added by way of the November 5, 2001 Preliminary Amendment.

In the March 17, 2003 Amendment (Paper No. 47) Applicants amended the specification to cancel the second paragraph of the Amendment to page 59-60 of the specification (*see* 05 November 2001 Amendment to Specification; Paper No. 37). However, Applicants have retained matter added in the November 5, 2001 amendment to the specification related to the ability of the 5G1.1 antibody to bind to both the alpha and beta chains of C5 as this language merely recites an inherent property of the 5G1.1 antibody, and does not add new matter to the specification.

> By disclosing in a patent application a device that inherently performs a function or has a property, operates according to a theory or has an advantage, a patent application necessarily discloses that function, theory or advantage, even though it says nothing explicit concerning it. The application may later be amended to recite the function, theory or advantage without introducing prohibited new matter. *In re Reynolds*, 443 F.2d 384, 170 U.S.P.Q. 94 (CCPA 1971); *In re Smythe*, 480 F. 2d 1376, 178 U.S.P.Q. 279 (CCPA 1973). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted).

Manual of Patent Examining Procedure, Eighth Edition ("M.P.E.P.") § 2163.07 (a), (emphasis added). *See also Jewish Hospital v. St. Louis v. Idexx Laboratories* (951 F.Supp. 2, 4, 42 U.S.P.Q. 2d 1720, 1723) (D. Maine 1996)

> The original application made clear that the applicant was claiming to have discovered and was seeking a patent for newly-defined antigens in dog blood or sera, new antibodies, and new tests for determining the

> presence of heartworm. For the antigens, the original claim listed six characteristics. The continuation-in-part added four more. These additional characteristics are inherent in the antigens originally discovered; they simply add more descriptive criteria...Since the continuation-in-part provides inherent characteristics of the items previously disclosed in the 1983 application, it does not result in a later effective date.

(emphasis added); *Kennecott Corp. v. Kyocera Int'l, Inc.*, 835 F.2d 1419, 1421-22 (Fed.Cir.1987) (entitling a description of the inherent property of an "equiaxed microstructure," though later added to the specification, to the original filing date because "anyone with a microscope would see the microstructure of the product."); *In re Nathan*, 328 F.2d 1005, 1009 (later added limitation to the claims that a class of 2-halo steroids had an "alpha orientation" was not new matter because the amendatory material was "concerned with an inherent characteristic of an illustrative product of applicants' invention already sufficiently identified in appellants' original disclosure as filed.").

The inherent property of the 5G1.1 antibody to bind both the alpha and beta chain of C5 is confirmed in the Wang *et al.* '642 patent discussed above. Thus, the inherent property of the 5G1.1 antibody would have been known to one of skill in the art at the time the application was filed. Because the characteristic of the 5G1.1 antibody to bind to both the alpha and beta chains of C5 is inherent in the antibody, it is simply a "more descriptive criterion" and does not add new matter to the specification. Furthermore, the characteristic of the 5G1.1 antibody to bind to both the alpha and beta chains of C5 "would be so recognized by persons of ordinary skill."

Accordingly, Applicants respectfully request that this objection be reconsidered and withdrawn.

II. Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 19-34 stand rejected under 35 U.S.C. § 112, first paragraph. The Examiner alleges that the specification does not contain written description of the claimed invention and does not reasonably convey to one of skill in the art that Applicants had possession of the claimed invention (Office Action, section 5).

Applicants respectfully traverse this ground of rejection.

The Examiner opines that "generic disclosure" of C5 blockers on pages 56 and 59-60 of the specification does not provide adequate written description support for the antibodies which "bind to the alpha chain of C5." However, Applicants respectfully direct the Examiner's attention to the Amendments to the specification submitted on November 5, 2001 (Paper No. 37, Appendix D) and March 17, 2003 (Paper No. 47, Appendix B). In light of these amendment, the specification on, *e.g.*, pages 59-60, now reads:

> The supernatant from a hybridoma designated as 5G1.1 tested positive by ELISA and substantially reduced the cell-lysing ability of complement present in normal human blood in the chicken erythrocyte assay. Further analyses revealed that the 5G1.1 antibody has two ~~surprising~~ properties: 1) it reduces the cell-lysing ability of complement present in normal blood so efficiently that, even when present at roughly one-half the molar concentration of human C5 in the hemolytic assay, it can almost completely neutralize serum hemolytic activity; and 2) it binds to both the alpha and beta chains of the human C5 protein.

(emphasis added). Thus, it will be appreciated that there is adequate written support in the specification for antibodies which bind the alpha chain of C5.

Additionally, the inherent property of the 5G1.1 antibody to bind both the alpha and beta chain of C5 is confirmed in the Wang *et al.* '642 patent discussed above. Thus, the inherent

property of the 5G1.1 antibody was known to one of skill in the art at the time the application was filed. Because the characteristic of the 5G1.1 antibody to bind to both the alpha and beta chains of C5 is inherent in the antibody, and because the Applicants were in possession of the 5G1.1. antibody, Applicants were also in possession of antibodies which "bind to the alpha chain of C5."

Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

III. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 18 has been rejected under 35 U.S.C. § 112, second paragraph, as lacking proper antecedent basis.

Applicants have amended claim 18 herein to depend upon claim 17.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

IV. Rejection Under 35 U.S.C. 102(b)

Claims 1-10, 14, 17-28, and 32-33 have been rejected under 35 U.S.C. § 102(b) over Larrick *et al.* (EP 0245993) (Office Action, section 9).

Applicants respectfully traverse this ground of rejection.

The Examiner cites Larrick *et al* as teaching antibodies that bind C5a. However, the antibodies of Larrick *et al.* are specific for human complement component C5a (see, *e.g.,* page 2, lines 1-2 and page 3, line 1-2). It is respectfully noted that C5a (as well as C5b) is a cleavage product of C5 (see, *e.g.,* specification, page 3, lines 5-6). That is, because the antibodies of Larrick *et al.* are specific for C5a, Larrick *et al.* does not disclose antibodies, which bind C5 and/or the alpha chain of C5.

Furthermore, Larrick *et al.* does not disclose a method for the treatment of established joint inflammation in a patient in need thereof comprising administering to the patient an effective anti-inflammatory amount of a composition comprising a purified antibody, which binds C5 and/or the alpha chain of C5, as claimed by the Applicants.

Accordingly, reconsideration and withdrawal of this ground of rejection is respectfully requested.

V. Rejection Under 35 U.S.C. 103(a)

Claims 1-14 and 17 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Sims *et al.* (U.S. Patent No. 5,635,178) (Office Action, section 10).

Applicants respectfully traverse this ground of rejection.

The Examiner appears to rely solely on the claims of Sims *et al.* The Examiner opines that Sims *et al.* claims methods and compositions comprising antibodies that specifically bind a component of C5b-9 complex, and that, given that C5b is a component of the C5b-9 complex,

the claimed methods of Sims *et al.* read on the instant claimed methods for the treatment of established joint inflammation comprising administering an effective amount of a composition comprising a purified antibody specific against C5 (Office Action, section 10).

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the...claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989) (emphasis added); *Datascope Corp. v. SMEC, Inc.*, 224 USPQ 694, 698 (D. N.J. 1984), *aff'd in part & rev'd in part*, 776 F.2d 320, 227 USPQ 838 (Fed. Cir. 1985) ("Anticipation cannot be predicated on teachings in a reference that are vague or based on conjecture") (emphasis added). *See also Ex parte Standish*, 10 USPQ2d 1454, 1457 (Bd. Pat. App. & Int'f 1989) ("anticipation of a claimed product cannot be predicated on mere conjecture as to the characteristics of a prior art product") (emphasis added).

Respectfully, Sims *et al.* does not teach a method for the treatment of established joint inflammation in a patient in need thereof comprising administering to the patient an effective anti-inflammatory amount of a composition comprising a purified antibody specific against C5, as claimed by the Applicants. For instance, Sims *et al.* teaches in the "Summary of the Invention" that the composition and methods of the invention are related to

> polypeptides having the ability to act as an inhibitor of complement C5b-9 activity. The compositions contain an 18 kDa protein found on the surface of human erythrocytes, a 37 kDa protein found on the surface of human platelets, a 37 kDa protein found on the surface of human endothelial cells, active derivatives or fragments thereof which act to inhibit the activity of C5b-9, anti-idiotypic antibodies mimicking the action of the

> inhibitor proteins or antibodies against C7 or C9 which block the formation of the C5b-9 complex.

Column 3, lines 30-40.

For instance, Sims *et al.* teaches a monospecific rabbit antibody against the purified human erythrocyte 18 kDa protein (α-P18) (Col. 7, lines 36-38). The α-P18 antibody binds to the 18 kDa protein on the erythrocyte membrane and prevents the C5b-9 complex from forming on the platelet surface (Col. 9, line 40).

Further, Sims *et al.* states that

> [a]s used herein in the compositions and methods for the prolongation of platelet and organ survival and enhancement of therapeutic efficacy or suppression of complement mediated disorders, "C5b-9 inactivator" refers to the 37 kDa protein from platelets, the corresponding 37 kDa protein on endothelial cells, the 18 kDa protein on erythrocyte membranes, peptide fragments thereof having C5b-9 inhibitory activity, and preferably containing a membrane binding domain, whether isolated from naturally produced materials or recombinantly engineered sequences, monoclonal antibodies to C7 that block membrane binding of the C5b-9, monoclonal antibodies to C9 that block C9 polymerization and insertion into the membrane, monoclonal antibodies that blocks C9 binding to C5b-9, and anti-idiotypic antibodies which inhibit the function of the cell surface molecules in inhibiting C5b-9 activity, especially the Fab fragments of monoclonal antibodies having this activity. All molecular weights are determined by SDS-PAGE under non-reducing conditions. The 37 kDa and 18 kDa proteins are species specific, i.e., only inhibitor proteins of human origin will inhibit human C5b-9.

Column 5, lines 30-51 (emphasis added).

However, nowhere does Sims *et al.* teach antibodies specific against C5. Similarly, nowhere does Sims *et al.* teach a method for the treatment of established joint inflammation comprising administering a composition comprising a purified antibody specific against C5.

Furthermore, even assuming *arguendo* that Sims *et al.* does teach an antibody which is specific for a component of the C5b-9 complex, as the Examiner contends, Sims *et al.* still does not teach the antibodies used in the methods of the claimed invention. C5b (like C5a) is a cleavage product of C5 (see, *e.g.,* specification, page 3, lines 5-6). That is, because the antibodies, which are (arguably) taught by Sims *et al.,* are specific for C5b (the component of the C5b-9 complex that the Examiner contends is at issue), Sims *et al.* does not disclose antibodies, which specifically bind C5. Thus, Sims *et al.* does not disclose a method for the treatment of established joint inflammation in a patient in need thereof comprising administering to the patient an effective anti-inflammatory amount of a composition comprising a purified antibody, which specifically binds C5, as claimed by the Applicants.

Thus, claims 1-14 and 17 are not anticipated by Sims *et al.* Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

VI. Rejection Under 35 U.S.C. 103(a)

Claims 1-14 and 17-34 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Larrick *et al.* (EP 0245993), in view of alleged "art known assays of testing complement" as taught by Auda *et al.* (Rheumatol. Int. 10:185-18 (1990)), Wurzner *et al.* (Complement Inflamm. 8:328-40 (1991)), Wang *et al.* (U.S. Patent No. 6,074,642) and Anderson *et al.* (*S. Alf. Med. J.* 59:666-689 (1981)).

This ground of rejection is respectfully traversed.

As discussed elsewhere herein Larrick *et al.* teaches antibodies that are specific for human complement component C5a (see, *e.g.*, page 2, lines 1-2 and page 3, line 1-2). It is respectfully noted that C5a (as well as C5b) is a cleavage product of C5 (see, *e.g.*, specification, page 3, lines 5-6). That is, because the antibodies of Larrick *et al.* are specific for C5a, Larrick *et al.* does not disclose antibodies, which bind C5 and/or the alpha chain of C5. In fact, Larrick *et al.* actually teaches away from the antibodies used in the methods of the claimed invention:

> [I]t is the C5a fragment, rather than the C5, which is to be inhibited because only C5a causes chemotaxis and neutrophil aggregation...[b]ecause C5a has no known enzymatic activity, specific binding thereto and direct neutralization thereof would appear to represent the best approach to combat the toxicity of the C5a mediator" (page 2, lines 46-52).

Therefore, Larrick *et al.* teaches antibodies specific for C5a and actually teaches away from the use of antibodies specific for C5 (or which bind the alpha chain of C5).

Furthermore, Larrick *et al.* does not teach or suggest a method for the treatment of established joint inflammation in a patient in need thereof comprising administering to the patient an effective anti-inflammatory amount of a composition comprising a purified antibody, which binds C5 and/or the alpha chain of C5, as claimed by the Applicants.

Additionally, as acknowledged by the Examiner, Larrick *et al.* also does not teach or suggest monitoring levels of C5a or C5b after administration of administration of antibodies which bind C5 or the alpha chain of C5[1], as recited, *e.g.*, in dependent claims 11 and 29. To

[1] The Examiner states that Larrick *et al.* differs from the claimed invention by not disclosing monitoring the levels of C5a and C5b after the administration of "C5/C5a-specific antibodies" (Office Action, section 11). Respectfully, the Examiner may be confusing antibodies that are specific for the C5a cleavage product and antibodies that bind the

supplement this deficiency, the Examiner cites Auda *et al.*, Wurzner *et al.*, Wang *et al.*, and Anderson *et al.* as teaching the various methods of monitoring complement activity. Auda *et al.* is cited to teach the measurement of complement activation products in patients with chronic rheumatic diseases. Wurzner *et al.* is cited to teach various assays to test the activity of complement complexes and components. Wang *et al.* is cited to teach that levels of complement activity in glomerulonephritis patients may be monitored by, *e.g.*, cell lysis assays or measuring of complement levels. Finally, Anderson *et al.* is cited to teach various assays to test the activity of complement, including chemotaxis.

However, even assuming *arguendo* that these supplemental references do teach various methods of monitoring complement levels, they do not supplement the deficiency of Larrick *et al.*, which actually teaches away from the use of antibodies specific for C5 (or which bind the alpha chain of C5) for the treatment of conditions associated with complement activation. Thus, Larrick *et al.* does not teach or suggest a method for the treatment of established joint inflammation in a patient in need thereof comprising administering to the patient an effective anti-inflammatory amount of a composition comprising a purified antibody, which binds C5 and/or the alpha chain of C5, as claimed by the Applicants.

Wang *et al.* is also cited to teach the "therapeutic effects of the anti-C5a antibody 5G1.1 of the instant application" (Office Action, section 11)[2]. The Examiner opines that given these

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alpha chain of C5. The antibodies used in the methods of the claimed invention are specific for C5 and/or bind the alpha chain of C5.

[2] Once again, it appears that the Examiner may be confusing antibodies that are specific for the C5a cleavage product and antibodies that bind the alpha chain of C5. The antibodies used in the methods of the claimed invention are specific for C5 and/or bind the alpha chain of C5. The 5G1.1 antibody disclosed in Wang *et al.* and in the instant application binds the alpha chain of the C5 protein (see specification, paragraph spanning pages 59-60, as amended).

asserted properties of the 5G1.1 antibody, one skilled in the art "would have been motivated to substitute the anti-C5 5G1.1 antibody in the methods of treating arthritis taught by Larrick *et al.*" (Office Action, section 11). However, as discussed elsewhere herein, Larrick *et al.* teaches the use of anti-C5a specific antibodies and actually teaches away from the use of antibodies that are specific for C5. Thus, because of the actual teachings of the Larrick *et al.* reference, one skilled in the art would not have had the requisite motivation to combine the references.

In fact, not one of these references, either alone or in combination with the other references, discloses or suggests to the ordinarily skilled person the desirability of the claimed invention.

Thus, Applicants submit that independent claims 1 and 19 are non-obvious in view of the teachings of Larrick *et al.* either alone or in combination with the alleged art known assays of Auda *et al.*, Wurzner *et al.*, Wang *et al.*, and Anderson *et al.* Similarly, claims 2-14 and 17-34, wherein they depend directly or indirectly upon independent claims 1 and 19, and thus contain all the limitations thereof, also satisfy the requirements of 35 U.S.C. § 103(a).

Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

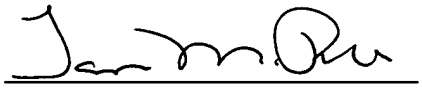
VII. Conclusion

In view of the foregoing remarks, Applicants respectfully submit that this application is now in condition for allowance. If a telephone interview would advance prosecution of the application, the Examiner is invited to call the undersigned at the number listed below.

A Petition for a one (1) month Extension of Time is filed concurrently herewith, which extends the period for response from November 12, 2003 to December 12, 2003. The Petition further authorizes the PTO to charge the one month extension fee of $110 to our Deposit Account No. 08-0219.

Applicants believe no other fees are due in connection with this Amendment. However, if there are any other fees due, please charge them to Deposit Account 08-0219. Also, please credit any overpayment to the same Deposit Account.

Respectfully submitted,



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